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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/381,556	01/05/2000	Yuman Fong	MSKP031USNP	4110

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OPPEDAHL AND LARSON LLP
P O BOX 5068
DILLON, CO 80435-5068

EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 05/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/381,556	FONG ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response received on 2/26/04 has been entered. New claims 41-56 have been added. Claims 1-56 are currently pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in a previous office action.

Double Patenting

Claims 1-22 and 38-40 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of U.S. Patent No. 6,051,428 (4/18/00), hereafter referred to as the '428 patent. Since the applicants have not traversed the grounds of rejection, the rejection of record stands. However, it is noted that applicants have again indicated their willingness to file a terminal disclaimer over US Patent 6,051,428 upon indication that the claims are allowable over the prior art of record.

Claim rejections - 35 U.S.C. 112

The rejection of claims 4-6 under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is maintained, and extended to include new claims 41-56 which depend on claim

4. The amendment to claim 4 and applicant's arguments have been fully considered but has not been found persuasive in overcoming the instant grounds of rejection for reasons of record.

The applicant argues that claim 4 has been amended to recite a step of "administering transduced tumor cells", thus overcoming the rejection of record. However, the amendment to claim 4 does not render the claims definite, and further renders claims 5 and 6 confusing and indefinite. Claim 5 recites the method according to claim 4, "..wherein the tumor cells are transduced with the amplicon *ex vivo,* further comprising the step of introducing the transduced tumor cells into the patient. Since claim 4 now already recites a step of administering the transduced tumor cells to the patient, it is unclear whether claim 5 is simply redundant, or whether the applicant intends to claim a second administration of the transduced tumor cells. Furthermore, claim 6 continues to recite the method according to claim 4, ".. wherein the amplicons are injected into the site of the tumor cells *in vivo*. Since claim 4 has been amended to include a step of administering transduced tumor cells to the patient, the limitation of claim 6 for direct transduction of the tumor cells *in vivo* is confusing as the limitations of claim 6 appear to conflict with the method of claim 4. It is suggested that the applicants separate the claims for *ex vivo* and *in vivo* transduction of tumor cells into 2 separate independent claims in order to more clearly claims the applicant's invention.

Claims rejections - 35 U.S.C. 101

The rejection of claims 36 and 37 under 35 U.S.C. 101 for non-statutory subject matter is withdrawn. However, it is noted for the record that claims 36 and 37 are interpreted to

encompass the transduced tumor cells themselves, and do not encompass or read on any host animal in which the tumor cells may reside.

Claims rejections - 35 U.S.C. 102

The rejection of claims 1-3, and 7-40 under 35 U.S.C. 102(e) over U.S. Patent No. 6,344,445, 2/5/02, hereafter referred to as Boursnell et al, is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

In regards to claims 1-3, and 7-37, the applicant argues that the Boursnell reference does not apply to the instant claims because Boursnell was not in "possession" of the invention. The applicant argues that Boursnell fails to demonstrate "possession" by failing to provide sufficient "written description" under 35 U.S.C. 112, first paragraph. The applicant further states that "written description" of the invention is separate from enablement.

In response, the MPEP at section 2121.01 sets forth the standard for determining whether the disclosure of a prior art reference meets the level of an anticipatory reference under 35 U.S.C. 102. MPEP 2121.01 states that "'In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'... .'" *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968). A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have

combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985). *In re Donohue* further states, " the fact that an author of a publication did not attempt to make the compound disclosed, without more, will not overcome a rejection based on that publication". Neither the MPEP nor *In re Donohue* discuss "written description" per se in regards to the disclosure of a prior art reference. Further, the case law cited by the applicants concerns the "written description" requirement as it pertains to the examination of applications for U.S. Patents for compliance under 35 U.S.C. 112, first paragraph, and not the "written description" requirement for anticipatory references under 35 U.S.C. 102. For the record, the teachings of the Boursnell reference have been evaluated as per MPEP 2121.01.

However, in regards to the cited case law, please note that *Moba B.V. v. Diamond Automation Inc.*, 66 USPQ2d 1429 (Fed. Cir. 2003), which provides extensive commentary on the earlier decisions of the *University of California v. Eli Lilly and Co.* and *Enzo Biochem Inc. v. Gen-Probe Inc.* , concludes that, "Compliance with written description requirement of 35 U.S.C. 112 does not require particular form of disclosure, provided a person of ordinary skill in the art could determine from specification that inventor possessed invention at time of filing" *Moba B.V. v. Diamond Automation Inc.*, page 1430. *Moba B.V. v. Diamond Automation Inc.* further cites *Union Oil Co. of Cal. v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000) for stating, " The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed'". see *Moba B.V. v. Diamond Automation Inc.*, page

1439. Nowhere in any of the cited cases is there the statement that an anticipatory reference must physically make the disclosed invention.

The applicant's grounds of stating that Boursnell lacks written description appears to be that Boursnell did not exemplify the structure of nucleotide sequences encoding two or more immunomodulatory proteins or provide information about the properties of these nucleotide sequences. Boursnell et al. however provides substantial direction for making mixtures of recombinant HSV amplicons and packaged HSV vectors which encode an immunomodulatory or therapeutic gene (Boursnell et al., column 14, lines 17-41, columns 16-23, Figures 1-6, and column 39-40). It is further noted that the claims in the Boursnell Patent in fact recite methods for using these recombinant HSV vectors to transduce cells (Boursnell et al., columns 39-40, claims 1-16). Specific immunomodulatory genes recited in the claims include IL-2, IL-12, and B7.1. Please note that under 35 U.S.C. 282, an issued U.S. Patent enjoys the presumption of validity. Case law further states, " Every patent is presumed valid .... The presumption of validity includes a presumption that the patent complies with 112" *National Recovery Technologies Inc. V. Magnetic Separation Systems Inc.,* 49 USPQ 1675 (Fed. Cir. 1999). Thus, as a matter of law, the Boursnell patent provides written description and enablement for HSV vectors comprising nucleotide sequences encoding immunomodulatory proteins.

Boursnell et al. further teaches that the HSV vectors may encode more than one genes, preferably one or more cytokines, or combinations of cytokines and costimulatory molecules (Boursnell et al., columns 7-8, and column 14, lines 54-60). Boursnell et al. also teaches that it was well within the skill of the ordinary artisan at the time of filing to make recombinant

vectors, including herpes vectors, that encode more than one immunomodulatory gene, such as an antigen and a cytokine (Boursnell et al., columns 2-3, bridging paragraph). From the detailed description in the Boursnell specification for making a recombinant HSV vector and from the clear indication by Boursnell that methods of making multiply recombinant herpes vectors were known in the art, the Boursnell et al. patent enables the disclosed mixtures of HSV amplicons and the use of those HSV amplicons and vectors to transduce tumor cells. Further, since Boursnell et al. provides sufficient written description for HSV vectors encoding an immunomodulatory molecule as evidenced by the claims in the Boursnell patent, and provided a clear description for making HSV vectors which encode more than one immunomodulatory molecule, Boursnell demonstrates possession of the invention as claimed in the instant application.

In regards to claims 38-40, the previous office action pointed out that these claims do not recite a combination of an immunostimulatory protein and a therapeutic gene and that as such claims 38-40 are directly anticipated by claims 12-14 of the Boursnell et al. patent. In response to the grounds of rejection over claims 38-40, the applicant has stated that they intend to file a Rule 131 declaration in regards to these claims. Since no such declaration has been received, the rejection of record stands.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. For all official communications, the technology center fax number is (703) 872-9306. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER